Amendments to the Specification:

A.

Please insert the following "Example 6" at the end of the present specification.

Example 6

The following example is included for illustrative purposes only and is not intended to limit the scope of the invention.

A blinded, randomized, placebo-controlled, multicenter study to assess the safety and efficacy of Dey Fluticasone Propionate Nasal Spray 50 mcg in adolescent and adult patients with seasonal allergic rhinitis was conducted. The primary objective of this study was to determine the safety and efficacy of Dey fluticasone propionate nasal spray 50 mcg (Dey-FP) compared with Placebo during 2 weeks of treatment in adult and adolescent patients with seasonal allergic rhinitis (SAR) due to mountain cedar pollen. The secondary objective was to establish the comparability of Dey-FP with FLONASE® Nasal Spray 50 mcg during 2 weeks of treatment in adults and adolescent patients with SAR due to mountain cedar pollen.

The study was a randomized, multicenter (7 sites), 3 treatment (Dey-FP, FLONASE®, and Placebo), 2 level (high and low dose) placebo-controlled repeated measures study conducted in the U.S. during the 2001/2002 mountain cedar pollen allergy season. The study duration was 3 weeks and consisted of 2 phases: a 1-week baseline screening period for diary data followed by a 2-week randomized patient- and rater-blind treatment phase. Patients were seen on an outpatient basis on Day-7, Day 1, Day 7, and Day 14. The initial baseline screening period for diary data began 1 week (Day-7.+-.2 days) prior to randomization to treatment. Patients who met the eligibility criteria (inclusion/exclusion criteria and completion of baseline study procedures [within 30 days of Day-7]) were assigned a patient number, given standard oral antihistamine as a rescue medication, and a Patient Total Nasal Symptom Score (TNSS) Diary. Patients recorded daily TNSS (sum of the signs and symptoms for runny nose, nasal congestion, sneezing, and itchy nose) in their diaries rating each on a scale of 0 to 3 with 0 being no

symptoms present and 3 being severe symptoms present. The amount of oral antihistamine taken was recorded as well.

One week later, at the conclusion of the baseline screening period, the patients returned to the study site and were re-evaluated for eligibility. Patients who did not complete the diaries or no longer met the entry criteria were discontinued. Patients who met all entry criteria were then randomized to 1 of 6 treatment groups: Dey-FP High Dose, Dey-FP Low Dose, FLONASE High Dose, FLONASE Low Dose, or Placebo High Dose or Placebo Low Dose. The patient- and rater-blind treatment phase (Day 1 through 14) consisted of once daily self-administered treatment (1-2 sprays into each nostril per administration). On Days 7 and 14 (or at early termination), patients returned to the study sites and were evaluated. Efficacy assessments included reflective and instantaneous TNSS daily diary information, patient and physician global evaluations, and use of rescue medication. Safety evaluations were the incidence of adverse events, clinical laboratory tests, physical examinations findings, vital signs measurements, and ECG results (see Study Flow Chart). Pollen counts, outside air temperature, rainfall, and humidity were also monitored and recorded by each study site.

A history of moderate-to-severe SAR due to mountain cedar pollen for at least 2 years individuals 12 years of age and older;

Confirmed IgE-mediated hypersensitivity to mountain cedar pollen within last 12 months (a positive result is required);

Minimum TNSS of 8 out of a maximum of 12 (either AM or PM 12-hour assessment) on at least 3 days during the baseline period, one of which must have been within 3 days of Day 1;

If receiving immunotherapy, a stable maintenance regimen for 30 days prior to study enrollment;

General good health and free of disease or concomitant treatment that could interfere with interpretation of study results;

Written informed consent/pediatric assent; and

Willingness to comply with study procedures.

Patients who met all criteria were then randomized to 1 of 6 treatment groups: (1) Dey-FP 50 mcg Low Dose (100 mcg)--1 spray in each nostril daily; (2) Dey-FP 50 mcg High Dose

(100 mcg)--1 spray in each nostril twice daily; (3) FLONASE® Nasal Spray Low Dose (100 mcg)--1 spray in each nostril daily; (4) FLONASE® Nasal Spray High Dose (200 mcg)--1 spray in each nostril daily twice daily; (5) placebo--1 spray in each nostril once daily; and, (6) placebo--1 spray in each nostril twice daily.

The primary endpoint for this study was the change from baseline in a patient's combined (AM and PM) 12-hour reflective TNSS over a 2-week treatment period. The primary endpoint analysis was the comparison of Dey-FP Low Dose versus Placebo High and Low Dose overall (Days 2-14) and at Days 7 and 14. TNSS consisted of the sum of the combined AM plus PM 12-hour assessment scores for runny nose, nasal congestion, sneezing, and itchy nose recorded twice daily on the Patient's TNSS Diary card. Baseline was defined as the average of the run-in period of the combined (AM plus PM) 12-hour reflective TNSS from the 7 calendar days .+-.2 days preceding Day 1.

Secondary endpoints for this study included:

The change from baseline in a patient's combined (AM plus PM) 12-hour reflective TNSS overall (Days 2-14);

The change from baseline in a patient's combined (AM plus PM) 12-hour reflective TNSS at Days 7 and 14;

The change from baseline in a patient's AM 12-hour reflective TNSS;

The change from baseline in a patient's PM 12-hour reflective TNSS;

The percent change from baseline in a patient's combined (AM plus PM) 12-hour reflective TNSS;

The percent change from baseline in a patient's AM 12-hour reflective TNSS;

The percent change from baseline in a patient's PM 12-hour reflective TNSS;

The change from baseline to 1-week and 2-week postbaseline in area under the curve (AUC) of patient's combined (AM plus PM) 12-hour reflective TNSS;

The change from baseline to 1-week and 2-week postbaseline in area under the curve (AUC) of patient's AM 12-hour reflective TNSS;

The change from baseline to 1-week and 2-week postbaseline in area under the curve (AUC) of patient's PM 12-hour reflective TNSS;

The change from baseline in patient's combined (AM plus PM) instantaneous TNSS;

The change from baseline in patient's AM instantaneous TNSS;

The change from baseline in patient's PM instantaneous TNSS;

Patient global evaluation of change in SAR signs and symptoms;

Physician global evaluation of change in SAR signs and symptoms; and

Use of rescue medication.

Secondary efficacy endpoints were compared across all treatment groups.

Both reflective and instantaneous change from baseline in 12-hour (AM plus PM, combined and individual) TNSS for primary and secondary variables were compared across treatment groups using a mixed effect analysis of variance (ANOVA) model with Treatment, day (Days 2-14) and the interaction of Treatment-by-Day as fixed effects and patients as random effect. Area under the curve (AUC) of the 12-hour (AM plus PM, combined and individual) reflective TNSS was calculated for the baseline period and Week 1 and Week 2 postbaseline using a trapezoidal method. The change from baseline in AUC was compared across the groups using a similar ANOVA model as described for the primary efficacy variable. Patient and physician global evaluations of change from baseline in SAR symptoms were compared between the groups using a one-way ANOVA model. Frequency of rescue medication use, as well as the percentage of patients needing rescue medication, was compared across the groups using the Pearson Chi-square test. The average number of tablets of rescue medication was compared using an ANOVA model. All statistical analyses were performed for both Intent-to-Treat (ITT) and Per Protocol (PP) Populations. TNSS missing observations in the ITT Population were imputed using the last observation carried forward (LOCF) method. All inferential statistics were conducted against a two-sided alternative hypothesis at 0.05 level of significance.

In all, 774 patients were enrolled and randomized to 1 of 6 treatment groups at 7 study centers located in the US during the 2001/2002 mountain cedar pollen allergy season, including 1 patient who enrolled at 2 separate sites (Patient 02-044 and 05-056 were the same patient). The data from Patient 02-044 were excluded from all analysis populations except the randomized patient population because the patient had received study drug. The data from Patient 05-056 were included in the analysis populations because enrollment at Site 5 preceded enrollment at the

second site, Site 2. The Intent-to-Treat (ITT) Population, therefore, was composed of 773 patients (774 randomized patients minus Patient 02-044). The distribution was as follows: 129 patients in the Dey-FP High Dose group, 129 in the Dey-FP Low Dose group, 127 in the FLONASE High Dose group, 129 in the FLONASE Low Dose group, 131 in the Placebo High Dose group, and 128 patients in the Placebo Low Dose group. In total, 752 (97.3%) patients of the original 774 completed the study and 22 (2.8%) discontinued prematurely, 8 of these were due to Aes. Patients were predominantly White (>90%) and female (>59%). The mean age range was from 37.55 to 42.01 years (min-max range=12.1 to 78.9 years) across treatment groups. Patients had a mean skin antigen challenge score of between 7.5 to 8.5 mm. Over half of all patients (>58%) had no previous history of fluticasone usage.

All active treatment groups (Dey-FP and FLONASE) demonstrated reductions in TNSS over the 2-week treatment period. Regardless of which efficacy endpoint was examined (i.e., 12-hour reflective TNSS, instantaneous TNSS, change in AUC), the Treatment effect was highly significant as was the day (duration of treatment) effect (p=0.0000) indicating improvement in TNSS. Both Dey-FP and FLONASE Low Dose groups were statistically superior to Placebos for both primary and secondary efficacy endpoint analyses, as were Dey-FP High Dose and FLONASE High Dose treatment groups. Treatment-by-Day interaction (overall Days 2-14) and Treatment-by-Week interaction (Week 1 and Week 2) effects were not statistically significant indicating that the treatment groups behaved similarly for the duration of the study, except for the magnitude of improvement in TNSS. There was no statistically significant differences between Dey-FP and FLONASE High and Low Dose groups for any efficacy endpoint analysis (relief of signs and symptoms of SAR). Moreover, all active treatment groups were consistently statistically superior to both High and Low Dose Placebo groups. Results of analyses for the Per Protocol Population paralleled those of the ITT Population for all efficacy variables.

In FIGS. 1-4, the efficacy of the nasal formulations is expressed as the change from baseline (pretreatment) in a composite score of nasal symptoms (e.g. runny nose, sneezing, nasal itching and congestion) referred to as total nasal symptom scores (TNSS). The change from baseline in TNSS scores is expressed in absolute units (rather tan percent change from baseline). Using an analysis of variance model (ANOVA), the least square mean (LS Mean) for the

baseline (positive value) and change from baseline (negative value if symptoms improve) are obtained. The higher the negative value seen in the LS Mean, the greater was the change (improvement) in TNSS.

Table 1 shows a particle size distribution of the fluticasone particles in Dey-FP, wherein the particle size is in microns. Table 2 also shows the particle size distribution of fluticasone particles of another batch of Dey-FP, wherein the particle size is in microns. Table 3 shows the formulation of Dey-FP.

Table 1

Dey-FP 50 mcg Particle Size Data – Batch 1				
	Run 1	Run 2	Run 3	Avg.
D (v,0.10)	0.38	0.38	0.41	0.39
D (v, 0.25)	0.75	0.75	0.78	0.76
D (v, 0.50)	1.50	1.51	1.56	1.52
D (v, 0.75)	2.93	2.94	3.05	2.97
D (v, 0.90)	5.22	5.21	5.42	5.28

Table 2

Dey-FP 50 mcg Particle Size Data – Batch 2				
	Run 1	Run 2	Run 3	Avg.
D (v,0.10)	0.38	0.42	0.37	0.39
D (v, 0.25)	0.76	0.79	0.72	0.76
D (v, 0.50)	1.53	1.57	1.40	1.50

D (v, 0.75)	3.00	3.08	2.64	2.91
D (v, 0.90)	5.34	5.50	4.53	5.12

Table 3

Formulation of Fluticasone Propionate Nasal Spray

Ingredient	Function	Drug Product Concentration	Per Spray	Per Bottle
Fluticasone Propionate USP	Active Ingredient	0.050% w/w	0.050 mg	8.00 mg
Benzalkonium Chloride Solution, 50% NF	Preservative	0.020% w/w	0.0388 mg	6.1 mg
Microcrystalline Cellulose/Carboxy-methylcellulose Sodium, NF	Suspending Agent	1.50% w/w	1.50 mg	240.0 mg
Polysorbate 80, NF	Wetting Agent	0.0050% w/w	0.005 mg	0.80 mg
Phenylethyl Alcohol, USP	Preservative	0.25% v/w	0.255 mg	40.80 mg
Dextrose, Anhydrous, USP	To adjust osmolality	5.00% w/w	5.00 mg	800.0 mg
Hydrochloric Acid, 1N	To adjust pH	As required	As required	As required
Purified Water, USP	Diluent	n/a	93.15 mg	14.90 g

The Figures and attachments herein are presented for illustrative purposes only. They are not intended to limit the scope of the invention. Further, it should be understood that various changes and modifications to the presently preferred embodiment described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the present invention and without diminishing its attendant advantages. It is therefore intended that such changes and modifications be covered by the appended claims. Also, the invention may suitably comprise, consist of or consist essentially of the elements or steps described herein. Further, the invention described herein suitably may

comprise or be practiced in the absence of any element or step which is not specifically disclosed herein. Further, one or more step described herein may be performed simultaneously with another step.

B.

Please insert the following new section ("Brief Description of the Figures") into the specification immediately prior to the "V. Detailed Discussion of the Invention". The "V. Detailed Discussion of the Invention" section begins at the top of page 6 of the present specification.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 shows the change from baseline in AM and PM reflective TNSS over time in the ITT population over a 14 day study period.

FIG. 2 shows the change from baseline in AM and PM reflective TNSS over time in the PP population over a 14 day study period.

FIG. 3 shows the change from baseline in AM reflective TNSS over time in the PP population over a 14 day study period.

FIG. 4 shows the change from baseline in PM reflective TNSS over time in the PP population over a 14 day study period.